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Global interlaboratory assessments of perfluoroalkyl substances under the Stockholm Convention on persistent organic pollutants

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ABSTRACT

The Global Monitoring Plan (GMP) according to article 16 of the Stockholm Convention on Persistent Organic Pollutants (POPs) requires that POP laboratories must be capable – at any time – to analyse samples for POPs within a variation of ±25%. Based on this target error of 25%, a statistical model using z-scores was applied to assess the performance of analytical laboratories for POPs and a number of matrices. Since the second round of these 'Bi-ennial Global Interlaboratory Assessment on Persistent Organic Pollutants (POPs)', carried out in 2012/2013, perfluoroalkyl substances (PFASs) have been included into the proficiency tests. The third round was carried out in 2016/2017. The test materials included test solutions of PFASs analytical standards, the abiotic matrices sediment, air (extract) and water and the biotic matrices fish, human milk and human plasma. The number of laboratories submitting results for PFASs remained quite stable (IL2 = 27 laboratories; IL3 = 29), but there was broader geographic distribution observed in IL3: in addition to the laboratories from Asia and the Western Europe/other groups, two laboratories from Africa participated, two from Central-Eastern Europe and one from the Latin American/Caribbean region.

Considering that PFASs were introduced for the first time in round 2, the results were good to reasonable compared to those of a number of other POPs included in the same study. However, it shall also be mentioned that for some matrices and PFASs, the number of laboratories submitting results was too small and the results too scattered to derive a consensus value. This was especially true for the PFOS precursor compounds and the air matrix. Also, laboratories struggle with the analysis of the branched PFOS isomers.

These interlaboratory assessments on PFASs gave promising results and demonstrated the importance of proficiency tests in an international environment to generate trust in laboratory results. The need to participate regularly in such intercomparison assessments is highlighted. The results show the current level of PFAS analysis, which varies by laboratory and by matrix rather than *per* geographic region.

1. Introduction

Interlaboratory assessments are an important tool to assess the performance of chemical analytical laboratories and to generate trust in their results. International proficiency tests have been recommended as a tool to assess the performance of laboratories analysing persistent organic pollutants (POPs) [1]. Participation in such assessments should be on a regular basis as stipulated in the guidance document for the Global Monitoring Plan on POPs under article 16 of the United Nations (UN) Stockholm Convention on Persistent Organic Pollutants [2]. Since the entry into force of the Stockholm Convention, the United Nations Environment Programme (UNEP; today named 'UN Environment') assists laboratories in developing countries through its capacity building projects to assess and, if possible, improve their performance. Since its beginning, the University of Örebro in Örebro, Sweden and the Free University Amsterdam (VU) in Amsterdam, the Netherlands organize the 'Bi-ennial Global Interlaboratory Assessment on Persistent Organic Pollutants (POPs)' as part of the UN Environment Programme's capacity building activities.

The first round of the Global Interlaboratory Assessment was implemented in 2010/2011 [3]. It was open to laboratories from

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developing and developed countries and included the initial twelve POPs in test solutions and various naturally contaminated test samples. In this first global assessment, 83 laboratories participated [3–5]. The second round – organized in 2012/2013 – had 89 laboratories participating and included the POPs listed by the Conference of the Parties to the Stockholm Convention in 2009 such as polybrominated flame retardants and perfluorinated alkyl substances (PFAS) [6,7]. In the third round (2016/2017), 175 laboratories registered and 133 delivered results for at least one group of POPs in one of the test materials [8]. This paper provides the results and interpretation for perfluorooctanesulfonic acid (PFOS) and some other perfluorinated alkyl substances (PFASs) such as various precursor compounds, perfluorinated acids or amides from the second and the third rounds of the 'Bi-ennial Global Interlaboratory Assessment on Persistent Organic Pollutants (POPs)'.

2. Materials and methods

2.1. Selection of participants

The laboratories were invited by UNEP. Many laboratories were known to UNEP and related to work for the Global Monitoring Plan (GMP) under the Stockholm Convention on POPs. A large number of laboratories was known to the organizers through academic networks or as participants in analytical sessions at international conferences and had shown an interest to participate.

2.2. Test materials

For the perfluorinated POPs, the groups of analytes in the test solutions and the six naturally contaminated samples to be analyzed for PFOS and additional perfluorinated compounds are shown in Table 1. The test solutions and air extracts were all homogeneous solutions. The dried sediment samples were obtained from the SETOC program [9] and the homogeneity of these samples was thoroughly tested under accreditation (ISO/IEC Guide 43, part 1), although not by analyzing PFAS concentrations but by different variables such as dry weight. The pike perch and crab test materials were prepared in the laboratory in Amsterdam. The homogeneity of the pike perch was tested for the polychlorinated biphenyls PCB 118 and PCB 153 and for a number of organochlorine pesticides. The CVs were 10% or lower. The crab homogeneity was tested with PFOS and showed a CV of 4.5%. The human milk was pooled into one large beaker (6 L in total) and stirred for 5–6 h; homogeneity testing was performed on five aliquots by analyzing for the main groups of POPs including OCPs, PCB, PCDD/PCDF, PBDE and PFOS. The human plasma pool was homogenized for 5 h and five aliquots tested for PFASs. The air extracts were obtained from active air samplers using polyurethane foams (PUF) and then extracted with either toluene or methanol depending on the class of POPs. Since concentrations of certain POPs, such as OCPs and PFASs in European air are low, the extracts have been spiked with certain OCPs and PFOS precursors.

2.3. Distribution of test samples

The test solutions of the analytical standards of PFOS, and PFASs and the test samples human milk, human blood and air extracts were distributed by the Man-Technology-Environment (MTM) Research Centre, Örebro University, Örebro, Sweden. The sediment, fish and the water samples were distributed by the Department Environment and Health (formerly Institute for Environmental Studies – IVM), VU University, Amsterdam, the Netherlands. All shipments containing human milk or blood samples were packed

Table 1
Test solutions of analytical standards and test samples for the analysis of PFAS in the 2nd and the 3rd rounds.

	2nd Round	3rd Round
Test solutions: Prepared, ampouled and labelled by Wellington Laboratories (Guelph, Canada)		
PFOS	A mixture of PFASs (PFCAs[a], PFSAs[b] and FOSA[c]), with PFOS and FOSA in the concentration range of 125 ng/g –320 ng/g in methanol.	A mixture of PFASs (PFOS, PFCAs, PFSAs, FOSAs and FOSEs) in methanol in the concentration range of 10 ng/g-500 ng/g.
PFAS	A mixture of PFOS precursors (MeFOSE[d], (EtFOSE)[e], MeFOSA[f], and EtFOSA)[g] in the concentration range of 630 ng/g-1,260 ng/g.	
Abiotic test samples		
Sediment	Samples were dried at 40°C, sieved (at 0.5 mm), homogenized, filled into plastic containers, and stored at room temperature until shipment. Samples were from WEPAL[h].	
	A marine sediment from the Netherlands.	A sediment from the Elbe River, Germany.
Air extract	PFOS and precursors were spiked to the extract. The extracts were ampouled into 1.2 mL amber glass ampoules before shipment.	
	A toluene extract of polyurethane foam (PUF) taken near one of Sweden's largest hazardous waste incinerators.	Air samples taken with active samplers in Barcelona, Spain, using PUFs conditioned and extracted with methanol.
Water	The water test materials consisted of surface water samples. After bottling in high-density polyethylene bottles (250 mL), the material was sterilized by irradiation.	
	Amsterdam harbour, the Netherlands.	Pooled, from different locations in the Netherlands.
Biotic test samples		
Fish	After filletting and homogenizing, individual glass screw cap jars were filled with ca. 50 g homogenate. The jars were sterilized by autoclaving, thus, could be stored and transported at room temperature before opening.	
	A pike-perch filet from the Netherlands.	Chinese mitten crab from the Netherlands.
Human milk	The test material consisted of pooled homogenized human milk from milk banks in Sweden. 50 mL milk was packed in polypropylene bottles and frozen prior to shipment.	
	Human milk from the Örebro region.	Human milk from the Örebro region.
Human blood	The human blood samples consisted of pooled human plasma from the general population and people occupationally exposed to PFASs. 1 mL of homogenized sample was placed in a polypropylene vial and kept frozen until shipment.	
	Occupationally exposed people were professional ski wax technicians.	Occupationally exposed people were firefighters.

[a] PFCAs: perfluoroalkyl carboxylic acids.
[b] PFSAs: perfluoroalkane sulfonic acids.
[c] FOSA: perfluorooctane sulphonamide.
[d] MeFOSE. N-methyl perfluorooctane sulfonamidoethanol
[e] EtFOSE: N-ethyl perfluorooctane sulfonamidoethano
[f] MeFOSA: N-methyl perfluorooctane sulfonamide.
[g] EtFOSA: N-ethyl perfluorooctane sulfonamide.
[h] WEPAL: Wageningen Evaluating Programmes for Analytical Laboratories.

in polystyrene containers with frozen plastic ice packs. Each shipment was accompanied by (a) a letter listing the type of test samples contained in the shipment, (b) a customs letter stating the context of the interlaboratory assessment, especially the technical nature and non-commercial approach, and (c) certificates on non-infectiousness of the materials, especially for the human milk and the human plasma samples.

2.4. Analytes

The analytes included linear and branched PFOS in the test samples and a larger spectrum of PFASs in the test solution of analytical standards. The human blood sample was intended for the analysis of PFOS with the option of analysing other PFASs.

2.5. Assessment of performance

All participating laboratories were provided with instructions and a template to report results for each of the POP groups electronically (MsExcel®). The laboratories were asked to use their own methods. The approach may result in somewhat more variation but avoids systematic errors that could be introduced when describing a standard method for all participants. All data received from the participants were entered into a database and assessed using a standard procedure to allow direct comparison between participants. The approach of the assessment is based on the standard ISO 13,528 (2005) and the International Union of Pure and Applied Chemistry International Harmonised Protocol for Proficiency Testing by Thompson et al. [10]. As for the first round of the Global Interlaboratory Assessment on POPs [3], the performance was assessed according to the QUASIMEME proficiency testing organisation (www.quasimeme.org). The assigned value, the between-lab CV values and the laboratory assessment using z-scores are based on the Cofino model [11] according to the principles employed in the Quality Assurance of Information for Marine Environmental Monitoring in Europe (QUASIMEME) proficiency testing. The following equation and definitions apply:

The formula used is:

$$z - \text{score} = \frac{\text{Mean from Laboratory} - \text{Assigned Value}}{\text{Total Error}}$$

The z-scores can be interpreted as follows:

$\|z\| < 2$	Satisfactory performance	S
$2 < \|z\| < 3$	Questionable performance	Q
$\|z\| > 3$	Unsatisfactory performance	U
$\|z\| > 6$	Extreme performance	U

We consider an assigned value reliable and statistically valid when certain criteria are met (for details see section 1.2 of the Appendix ('Supplementary information'). It is important to note that, in contrast with many other interlaboratory exercises, but in line with the requirement from the Global Monitoring Plan (GMP) of the Stockholm Convention, all laboratories producing results for the GMP of the Stockholm Convention should be able to distinguish between two values differing 50% from each other. Consequently, we have set a target error of 25% on which the z-scores are based.

In the results tables (from Tables 3–5), the last column for each round shows the "inclusion rate". This value is a percentage that reflects how many of the data are included in the between-laboratory CV, shown in the column to the left of the inclusion rate column. The higher the inclusion rate, the lower the number of outliers. A higher inclusion rate also tells that the between-laboratory relative standard deviation (RSD) is more representative of the entire group of participants that produced that specific matrix-determinant combination.

3. Results and discussion

3.1. Participation of laboratories

The participation of laboratories analyzing PFASs in the second or third round according to UN region is shown in Table 2. Also shown is the distribution of laboratories analyzing the different types of the test samples including the core matrices of the Global Monitoring Plan, i.e., air (A), human milk (HM) and water (W). Additional matrices of interest included human plasma (HP), fish (F), and sediment (Sed). It can be seen that the analytical capacity is mainly located in the 'Western Europe and other groups' (WEOG) and in the Asia-Pacific regions, capacities build up in other regions were seen in the 3rd round.

The number of participating laboratories in both rounds was very similar with 27 laboratories in the 2nd and 29 laboratories in the 3rd round. Whereas in both rounds, most laboratories were from the Asia (14 *vs.* 10 in IL2 *vs.* IL3) and the WEOG (13 *vs.* 14 in IL2 *vs.* IL3) regions, in the 2nd round no laboratories from Africa, Central Eastern European (CEE) or countries from the Group of Latin-America and the Caribbean (GRULAC) requested samples or reported results. Of the Asian laboratories, ten were located in China (one of them in Hong Kong), Japan (3) and the Republic of Korea (1). Water (20), fish (19) and sediment (18) were the most frequently analyzed types of test samples (Table 2).

For the 3rd round, 29 laboratories from all five UN regions delivered results for PFASs. New capacities have been built with two laboratories from Africa and CEE each and one laboratory from GRULAC. On the other hand, two laboratories from Japan, the Korean laboratory and four laboratories in China for unknown

Table 2
Regional distribution of laboratories reporting PFAS results in the second (IL2) and third (IL3) round of the UNEP-coordinated biennial assessment of POPs laboratories.

Region	2nd Round								3rd Round							
	Total	TS	Sed	Air	W	F	HM	HP	Total	TS	Sed	Air	W	F	HM	HP
Africa	–	–	–	–	–	–	–	–	2	2	2	1	2	1	–	
Asia	14	13	10	3	11	9	3	4	10	9	5	3	6	5	3	6
CEE	–	–	–	–	–	–	–	–	2	1	1	–	1	1	–	
GRULAC	–	–	–	–	–	–	–	–	1	1		1	1		–	
WEOG	13	9	8	6	9	10	5	5	14	14	9	6	9	8	3	6
Total	27	22	18	9	20	19	8	9	29	27	17	11	19	15	6	12

Total: Total number of laboratories that submitted results; TS: test solution of analytical standards; Sed: sediment; W: water, F: fish, HM: human milk, HP: human plasma; CEE: Central and Eastern Europe; GRULAC: Group of Latin American and Caribbean; WEOG: Western European and Other Groups.

Table 3
Summary of results for test solutions of analytical standards (Test Solutions I and J, for IL2 and Test Solution N for IL3) (ng/g). TC = Theoretical concentration, AV = Assigned value, NAV = No assigned value. LB = Lower bound, UB = Upper bound.

Test solution	IL2							IL3							
	n	AV (ng/g)	Mean (ng/g)	Min. (ng/g)	Max. (ng/g)	Btw-lab. CV (%)	Inclusion rate (%)	n	TC (ng/g)	AV (ng/g)	Mean (ng/g)	Min (ng/g)	Max (ng/g)	Btw-lab CV (%)	Inclusion rate (%)
L-PFOS	22	175	175	12	210	8	73	25	241	242	242	166	454	19	78
br-PFOS								**15**	48.2	47.5	47.5	30.9	176	**22**	66
tot-PFOS LB								**17**		300	300	198	381	**12**	67
tot-PFOS UB								**17**		299	299	198	381	**11**	67
FOSA	**13**	320	320	255	446	**3**	65	**14**	316	279	279	8.28	632	**30**	69
MeFOSA	**7**	807	807	489	1300	**41**	78	**8**	631	509	509	314	677	**31**	82
EtFOSA	**4**	NAV	1035	596	2500	**44**	67	**9**	316	NAV	233	64.4	311	**51**	79
MeFOSE	**5**	NAV	1202	584	2500	**3**	56	**7**	631	532	532	377	845	**27**	75
EtFOSE	**5**	NAV	632	599	1130	**11**	58	**6**	316	275	275	164	335	**28**	80
PFOS prec. LB								**6**		1812	1812	1139	2227	**25**	78
PFOS prec UB								**6**		1812	1812	1139	2227	**25**	78
PFBA	**13**	122	122	108	158	**11**	75	**17**	126	115	115	92.4	12,914	**17**	70
PFPeA	**10**	130	130	107	167	**16**	81	**19**	126	120	120	64.0	205	**20**	74
PFHxA	**16**	249	249	215	295	**3**	64	**24**	253	223	223	109	342	**19**	75
PFHpA	**16**	130	130	107	264	**10**	69	**24**	126	114	114	74.0	241	**21**	73
PFOA	**18**	128	128	106	142	**9**	80	**24**	253	239	239	171	370	**20**	81
PFNA	**17**	129	129	93	146	**11**	80	**25**	126	117	117	98.0	203	**11**	68
PFDA	**17**	247	247	220	288	**5**	64	**25**	126	118	118	75.0	217	**14**	72
L-PFBS	**13**	265	265	110	311	**12**	71	**21**	156	144	144	104	328	**12**	69
L-PFHxS	**17**	174	174	142	240	**8**	68	**24**	119	115	115	60.0	178	**13**	70
PFCAs + PFSAs LB								**16**		1314	1314	1073	14,358	**18**	70
PFCAs + PFSAs UB								**16**		1314	1314	1073	14,358	**18**	70
PFUnDA	**15**	124	124	111	145	**7**	70	**21**	NC	NAV	0.08	0.16	9.00	**167**	48
PFDoDA	**12**	128	128	112	190	**13**	73	**21**	NC	NAV	NAV	8.00	8.00	**NAV**	NAV
PFTrDA	**10**	131	131	78	148	**9**	71	**19**	NC	NAV	NAV	3.57	3.57	**NAV**	NAV
PFTeDA	**10**	136	136	105	159	**14**	78	**18**	NC	NAV	NAV	0.29	0.40	**NAV**	NAV
L-PFHpS	**4**	181	181	168	199	**9**	80	**9**	NC	NAV	NAV	0.12	0.12	**NAV**	NAV
L-PFDS	**11**	172	172	160	203	**8**	78	**18**	NC	NAV	0.08	0.10	191	**85**	51

In bold are the numbers of laboratories (n) submitting results and the Between Laboratory CV, which should be <25 (for satisfactory results).

reasons did not participate in the 3rd round. It should be noted that the vast majority of the Asian PFAS laboratories is found in China with six laboratories followed by Vietnam (2) and Japan (1). Within the WEOG region, the capacity was quite evenly distributed with three laboratories in Canada, two in Germany and Norway, and one laboratory in Australia, Spain, Finland, the Netherlands, Sweden, and the United States of America. Most laboratories submitted results for water (19), one of the core matrices of the GMP. For the

Table 4
IL2 and IL3 – Summary of results for abiotic matrices: sediment, air extract and water. AV = Assigned value.

Round of interlab/Test matrices Analytes	IL2							IL3						
	n	AV (ng/g)	Mean (ng/g)	Min. (ng/g)	Max. (ng/g)	Btw-lab. CV (%)	Inclusion rate (%)	n	AV (ng/g)	Mean (ng/g)	Min. (ng/g)	Max. (ng/g)	Btw-lab. CV (%)	Inclusion rate (%)
Sediment														
L-PFOS anion	**18**	7.99	7.99	6.00	11.8	**15**	71	**16**	0.65	0.65	0.46	5.71	**20**	63
br-PFOS anion								**10**	0.12	0.12	0.11	1.80	**17**	52
tot-PFOS LB								**11**	0.76	0.76	0.00	3.23	**13**	67
tot-PFOS UB								**11**	0.79	0.79	0.65	3.23	**23**	62
FOSA	**10**	0.28	0.28	0.16	0.85	**46**	68							
Air extract														
L-PFOS anion	**8**	10.7	10.7	4.74	99.2	**39**	59	**11**	11.8	11.8	9.36	34.9	**31**	67
br-PFOS anion								**5**	NAV	NAV	0.37	8.02	**NAV**	NAV
tot-PFOS LB								**10**	11.2	11.2	9.36	42.9	**26**	68
tot-PFOS UB								**6**	NAV	11.7	10.8	42.9	**23**	60
FOSA	**7**	6.40	6.40	0.15	9.32	**27**	60	**8**	NAV	23.0	7.60	63.2	**58**	72
MeFOSA	**3**	NAV	23.0	18.0	26.6	**19**	82	**5**	NAV	37.7	15.1	114	**98**	80
EtFOSA	**3**	NAV	27.5	19.0	27.8	**2**	64	**6**	NAV	81.6	20.9	282	**99**	74
MeFOSE	**3**	NAV	62.6	53.9	68.0	**11**	79	**6**	NAV	104	37.0	184	**57**	81
EtFOSE	**3**	NAV	62.3	51.5	63.0	**3**	64	**5**	NAV	46.6	44.9	100	**13**	58
PFOS prec LB								**5**	NAV	311	178	688	**4**	55
PFOS prec UB								**5**	NAV	311	178	688	**4**	55
Water														
L-PFOS anion	**20**	4.28	4.28	3.20	31.0	**21**	65	**19**	7.4	7.4	4.07	44.5	**33**	60
br-PFOS anion								**11**	NAV	3.9	1.40	15.6	**73**	69
tot-PFOS LB								**11**	10	10	5.35	60.1	**41**	61
tot-PFOS UB								**11**	10	10	7.29	60.1	**39**	63
FOSA	**5**	NAV	0.26	0.10	1.08	**115**	61							

In bold are the numbers of laboratories (n) submitting results and the Between Laboratory CV, which should be <25 (for satisfactory results).

Table 5
IL2 and IL3 – Summary of results for biotic matrices: fish, human milk and human plasma (all product basis). AV = Assigned value.

Round of interlab/Test matrices Analytes	IL2							IL3						
	n	AV (ng/g)	Mean (ng/g)	Min. (ng/g)	Max. (ng/g)	Btw-lab. CV (%)	Inclusion rate (%)	n	AV (ng/g)	Mean (ng/g)	Min. (ng/g)	Max. (ng/g)	Btw-lab. CV (%)	Inclusion rate (%)
Fish														
L-PFOS anion	19	13.4	13.4	10.2	20.1	13	71	14	7.85	7.85	0.89	18.4	4	59
br-PFOS anion								10	0.56	0.56	0.24	3.55	56	59
tot-PFOS LB								11	8.31	8.31	4.44	16.1	4	70
tot-PFOS UB								11	8.43	8.43	4.44	16.1	3	74
FOSA	13	2.25	2.25	1.67	3.00	18	74							
Human milk														
L-PFOS anion	8	0.0449	0.0449	0.0135	0.130	25	62	6	0.03	0.03	0.01	0.07	20	59
br-PFOS anion								5	NAV	0.01	0.01	0.02	6	65
tot-PFOS LB								5	0.04	0.04	0.04	0.07	12	74
tot-PFOS UB								5	0.04	0.04	0.04	0.10	12	74
FOSA	0	NAV	NAV	NAV	NAV	NAV	NAV							
Human plasma														
L-PFOS anion	8	7.89	7.89	5.53	12.51	34	76	12	3.47	3.47	3.08	4.44	7	67
br-PFOS anion								10	2.00	2.00	0.63	5.26	35	73
tot-PFOS LB								10	5.52	5.52	4.24	9.70	16	72
tot-PFOS UB								10	5.59	5.59	4.24	9.70	19	76
FOSA	0	NAV	NAV	NAV	0.00	NAV	NAV	6	NAV	NAV	0.003	0.003	NAV	NAV
PFBA	3	NAV	2.63	2.23	3.10	19	86	6	NAV	NAV	0.45	0.45	NAV	NAV
PFPeA	0	NAV	NAV	NAV	NAV	NAV	NAV	7	NAV	NAV	NAV	NAV	NAV	NAV
PFHxA	6	0.28	0.28	0.22	0.36	26	82	11	NAV	NAV	NAV	NAV	NAV	NAV
PFHpA	7	1.15	1.15	0.84	1.36	22	78	11	NAV	NAV	NAV	NAV	NAV	NAV
PFOA	9	72.7	72.7	50.5	80.0	10	75	11	1.18	1.18	0.42	1.86	24	71
PFNA	7	5.31	5.31	5.25	7.00	4	57	11	0.48	0.48	0.29	0.95	18	72
PFDA	7	3.44	3.44	3.16	4.60	10	72	11	0.17	0.17	0.14	0.25	12	72
PFCAs + PFSAs LB								8	NAV	NAV	0.11	0.11	NAV	NAV
PFCAs + PFSAs UB								11	1.84	1.84	1.44	2.33	10	70
PFUnDA	7	0.50	0.50	0.39	0.69	21	78	6	3.85	3.85	2.40	4.88	25	80
PFDoDA	7	0.67	0.67	0.56	1.07	26	83	6	NAV	4.72	2.80	10.9	46	69
PFTrDA	4	0.18	0.18	0.13	0.23	32	67	11	0.16	0.16	0.12	0.29	12	54
PFTeDA	5	NAV	0.44	0.20	0.76	55	75	11	NAV	NAV	0.02	0.02	NAV	NAV
L-PFBS	2	NAV	NAV	0.02	0.10	NAV	NAV	9	NAV	0.02	0.02	0.03	25	80
L-PFHxS	7	0.90	0.90	0.78	1.20	16	72	9	NAV	NAV	NAV	NAV	NAV	NAV
L-PFHpS	1	NAV	NAV	0.29	0.29	NAV	NAV	4	NAV	0.14	0.12	0.17	21	64
L-PFDS	0	NAV	NAV	0.00	0.00	NAV	NAV	9	NAV	NAV	0.21	0.21	NAV	NAV

other two core matrices – ambient air (11) and human milk (6) – less capacity was found but more than during the 2nd round. It shall be noted that more laboratories submitted results for human plasma (12) than for human milk. The environmental matrices sediment (17) and fish (15) were quite frequently analyzed (Table 2).

All participating laboratories used in-house methods for sample preparation, clean-up, extraction and instrumental analysis. It shall be noted that not all laboratories provided information on their methods according to the reporting format. The sample extraction, clean-up and detection of the more polar PFASs compounds, the perfluoroalkyl carboxylic and sulfonic acids, including PFOS, are completely different from those used for the 'traditional' lipophilic POPs. In both rounds the extraction of PFASs was mostly performed with liquid-liquid extraction (LLE), LLE in combination with ultrasonic, or solid phase extraction (SPE), which is in line with the study of Feng et al. [12]. Only three labs in IL2 reported to have used pressurized liquid extraction (PLE) for sediment and for fish, while no lab reported to have used PLE in IL3. For the extraction of the water sample, only one lab in IL2, and one lab in IL3 reported to have used LLE and two labs in IL3 reported to have used filtration or dilution for extraction of PFAS from water. For the extraction of water the predominantly used method in both rounds was SPE, which is the recommended method of the ISO standard 25101:2009 [13].

In both rounds, the majority of participants used methanol or acetonitrile-based extraction solvents, although for water only one lab in IL2 used acetonitrile, and for sediment only three labs in IL3 used acetonitrile.

Cleaning of the extracts or fractionation was often performed by SPE for all matrices. Dispersed active carbon was used by some laboratories for the cleaning of the fish or the sediment samples.

From the 25 laboratories that submitted results for PFAS in the second round only one laboratory used a time-of-flight mass spectrometer (TOF-MS) for detection; and from the 29 laboratories of the 3rd round only one laboratory used a QTOF-MS, all others reported to have used LC/MS/MS. For the separation of the analytes, the majority used C_{18} based HPLC columns (IL2: n = 20, IL3: n = 20); however, some also used C_8-based columns (IL2: n = 3, IL3: n = 6), or another type of column (IL2: n = 2, IL3: n = 3). One laboratory reported to have applied GC/LRMS (using a DB-WAX 147 column, 30 m × 0.25 mm × 0.25 μm) for the separation of PFOS precursors, e.g., Me/EtFOSA and Me/EtFOSE.

Due to the large number of parameters, there is not one method or set of methods that clearly stands out. In that sense no clear suggestion for a preferred method could be given.

3.2. Quantitative results

3.2.1. Test solutions of analytical standards

The results from the second and the third interlaboratory assessment (IL2, IL3) for the PFAS compounds in the standard solutions are summarized in Table 3. The table includes the assigned values (AV) for each of the analytes and for the 3rd round also the theoretical concentration (TC); i.e. the concentration given by the laboratory that prepared the mix of the test solution. The detailed results by laboratory and the associated z-scores together with the

color-coded interpretation are provided in the 'supplementary information' in Tables S1 and S2 for IL2 and Tables S15 and S16 for IL3.

22 or 25 laboratories submitted results in the IL2 or L3, respectively. The number of laboratories that analyzed the PFOS precursor compounds (FOSAs and FOSEs) is much smaller than the number of laboratories that analyzed the carboxylic acids and the sulfonates. It shall be noted that in the 3rd round six of the PFASs were not contained in the test solution but were reported by a number of laboratories (PFUnDA, PFDoDA, PFTrDA, PFTeDA, L-PFHpS, L-PFDS).

In general, the results as coefficient of variation (CV) were excellent in both rounds and for all analytes. Most of them were below 25%, corresponding to 2 z−scores and even below or at around 10%, which is often taken as a stricter performance requirement for 'pure' test solutions. Relatively high CVs were obtained within the group of the PFOS precursor compounds and especially for the FOSAs (CVs 27%−51%). It is noteworthy that very good compliance (>95%) between the TC and the AV was achieved for analytes like L-PFOS, br-PFOS, PFPeA, and L-PFHxS. For the PFOS precursors, for EtFOSA no AV could be determined and for the other precursors - FOSA, MeFOSA, MeFOSE, EtFOSE, PFHxA - the difference between TC and AV was greater than 10%, indicating that the analysis of the precursor compound is more difficult and not so commonly performed.

3.2.2. Abiotic test samples: sediment, air and water samples

For the abiotic matrices, analytes differed between IL2 and IL3: In IL2, laboratories were asked to analyse the linear PFOS (L-PFOS) and the precursor compound FOSA; in IL3, the analytes comprised the L-PFOS and the branched PFOS (br-PFOS) as a group. The difference is due to the development under the Stockholm Convention where it was recommended to analyse the precursor compounds only in air but report L- and br-PFOS separately and as a sum. Therefore, sum parameters were assessed in IL3 only. The summary results are displayed in Table 4 for the sediment, air and water samples. The detailed results by laboratory and the associated z-scores together with the color-coded interpretation are provided in the 'supplementary information' for the sediment samples in Tables S3 and S4 for IL2 and Tables S17 and S18 for IL3; for the air samples in Tables S5 and S6 for IL2and Tables S19 and S20 for IL3; and for the water samples in Tables S8 and S9 for IL2 and Tables S21 and S22 for IL3. The CVs for FOSA in sediment and water are based on a few laboratories only (10 or 5 for IL3 and IL3, resp.) and would result in unsatisfactory results (CVs >45) and are not discussed further.

The summary CVs for various parameters of PFOS the sediment samples in IL2 and IL3 were all satisfactory with values between 13 and 20. In IL2, only two laboratories had z-scores slightly above 3 for L-PFOS (Table S4). In the IL3, it shall be noted that the CV = 17 (n = 10) for the br-PFOS was slightly better than the CV = 20 for the L-PFOS (n = 16). However, some laboratories struggle with the analysis of both groups of isomers and fail to report satisfactory results (see Table S18).

The fortified air extracts were analysed by nine or eleven laboratories only (Table 2). All of them struggle with the analysis of br-PFOS (in IL3) and the PFOS precursors (in both) (Table 4). In IL2, only three results were submitted for the PFOS precursors (MeFOSA, EtFOSA, MeFOSE, and EtFOSE), which made statistical evaluation unfeasible. In IL3, no AVs could be determined for br-PFOS or any of the PFOS precursors and a consensus value could be assigned for the L-PFOS only (11.8 ng/g). It can be seen from Table S19 that also for L-PFOS the results varied largely and the z-scores were either excellent or unsatisfactory (Table S20).

For the water sample, 20 laboratories submitted results in IL2 and 19 laboratories in IL3 (Table 2). All but one laboratory reported results for L-PFOS but only eleven for br-PFOS (in IL3); one laboratory was a total outlier (Table S22). In summary, the results for L-PFOS were satisfactory (CV = 21% in IL2) and quite good (CV = 33% in IL3) (Table 4). For the br-PFOS, the variation was larger (CV = 73) and the number of laboratories reporting results lower (n = 11).

3.2.3. Biotic test samples: fish, human milk and human plasma

For the biotic matrices, analytes differed between IL2 and IL3 as was for the abiotic samples. For human plasma, the full spectrum of PFASs as shown in Table 3 was to be reported. The summary results are displayed in Table 5 for fish, human milk and human plasma. The detailed results by laboratory and the associated z-scores together with the color-coded interpretation are provided in the 'supplementary information' for the fish samples in Tables S9 and S10 for IL2 and Tables S23 and S24 for IL3; for the human milk samples in Tables S11 and S12 for IL2and Tables S25 and S26 for IL3; and for the human plasma samples in Tables S13 and S14 for IL2 and Tables S27 and S28 for IL3.

The fish samples were analyzed by the largest number of laboratories: 19 in IL2 and 14 in IL3. In both rounds, the results for the L-PFOS were excellent as demonstrated by the low CVs: the between laboratory variation was 13% in IL2 and 4% in IL3 (Table 5), which also resulted in low CVs for the PFOS total (tot-PFOS) at upper bound (UB) and lower bound (LB) limits. The number of laboratories that reported br-PFOS (in IL3) was lower (n = 10) and the performance was poorer (CV = 56). Comparison of the individual laboratory results in Tables S10 and S24 show that in IL3 two laboratories had extreme unsatisfactory results (z-score > 6) and one laboratory only determined tot-PFOS. In IL2, there was only one laboratory with an unsatisfactory result (z-score = 3.97).

Only a limited number of laboratories analysed PFOS in human milk; i.e. eight laboratories in IL2 and 6 laboratories in IL3. The interlaboratory variations was for L-PFOS were acceptable with a CV of 25% in IL2 and satisfactory with a CV = 20 in IL3 (Table 5) for this complex analysis and concentrations close to the detection limit of most laboratories.

For the human plasma sample (Table 5) − a matrix more commonly used than human milk − a total of 17 PFASs should be reported. An increase in the number of reporting laboratories could be observed when comparing IL2 (n = 8 + 1 lab for PFOA) with IL3 (n = 12) but still low in comparison with other POPs or matrices. Only a limited number of laboratories presented results and for about half of the analytes an AV could not be determined. The performance of the laboratories in IL2 were reasonable with CVs varying from 4% (PFNA, n = 7) to 55% (PFTeDA, n = 5); for L-PFOS the CV was not satisfactory (CV = 34). In IL3, a better performance was seen with a CV of 7% for L-PFOS (n = 12) but CV = 35% for br-PFOS (n = 10).

3.3. z-scores

In the 2nd round (IL2), a total of 10,850 results met the statistical criteria of the assessment so that z-scores could be assigned to the results submitted by 89 laboratories. Of these, 442 (corresponding to 4% of all) were for PFAS. In the 3rd round (IL3), a total of 13,255 POP results submitted by 133 laboratories could be assigned z-scores; of these, 630 (corresponding to 5% of all) were for PFAS. This number is quite small when compared to 5,897 (or 44% of all in IL3) z-scores that were obtained for the dioxin-like POPs (polychlorinated dibenzodioxins, polychlorinated dibenzofurans and dioxin-like PCB). In Table 6 it can be seen that overall the results submitted in IL2 were slightly better than for IL3: In IL2, 85% of z-scores were 'satisfactory' ('S', n = 377), 4% 'questionable' ('Q', n = 39) and 9% 'unsatisfactory' ('U', n = 19). For IL3, the assessment is as follows: 73% of the results were 'S' (n = 461), 14% were 'Q'

Table 6
Overview of z-score results for PFAS in IL2 and IL3.

PFAS	# S	# Q	# U	# C	# I	Total	% S	% Q	% U	% C	% I
IL2	377	39	19	3	4	**435**	85	4	9	1	1
IL3	461	64	89	8	8	**630**	73	14	10	1	1

(n = 64), and 10% were 'U' (n = 89). 'C' and 'I' results are either 'consistent' or 'inconsistent' for values reported below the limit of quantification according to the model [11].

The Figs. 1–3 provide information as to the laboratory's performance – as percentage variation of the CV – in the two rounds of interlaboratory assessments. Fig. 1 shows that the performance of the analysis of L-PFOS improved from IL2 to IL3 for the fish, human milk, human plasma and air extract samples but decreased for the test solution, sediment and water. The overall performance level for L-PFOS was excellent to reasonable since most CVs were below the UNEP criterion of 25%.

The performance for other PFASs that are not yet listed under the Stockholm Convention in the test solutions and the human blood samples is shown in Fig. 2. Overall, the performance is excellent and higher CVs were obtained only for PFUnDA and L-PFDS.

For the precursor compounds – Me-/Et-FOSA/-FOSE and FOSA –the results are less impressive. For br-PFOS (assessed only in IL3), no AV could be determined for the air extract at all and for the test solution, the CV was 22%. Quantification of PFOS analyzed by LC-MS/MS is typically performed on either the mass transition 499 → 99 or 499 → 80. The ratio of those two mass transitions and the abundance of the MS/MS fragments vary *per* isomer, which may cause over- or underestimation of the total concentrations of PFOS when quantified with either a technical mixture of PFOS isomers or a standard containing 100% pure linear PFOS [14].

When the linear PFOS isomer is chromatographically separated from the other PFOS isomers, it would be possible to perform an accurate quantification of linear PFOS based on a 100% pure linear PFOS standard solution.

The occurrence of PFASs isomers in matrices differ not only *per* type of matrix, but also between samples of the same matrix. The difference in isomer patterns, in combination with the isomer specific response factors are making it impossible to perform an accurate quantification of the sum of isomers, based on either a technical mixture or a 100% pure linear PFOS standard solution.

For accurate quantification of branched isomers it is needed to quantify each isomer separate with isomer specific quantification solutions, and chromatographic conditions need to be optimize so all isomers would be baseline separated.

Most laboratories performing PFASs analyses do not have all PFOS isomers chromatographically separated, and have not used separate branched isomer standard solutions *per* isomer. To compare performance of laboratories on the analyses of the sum of br-PFOS, it would be needed that all laboratories use the same quantification standard. However, within the scope of the present study laboratories were requested to use their in-house methods to mimic their performance on routine analyses for analyzing samples for their agreement within the Stockholm Convention.

The comparison between IL2 and IL3 for L-PFOS and the precursors are shown in Fig. 3. Overall, the results were quite promising with many CVs below the 'UNEP' criterion of 25%. Interestingly, the performance – as % CV – for almost all types of test samples decreased from IL2 to IL3 so that in IL3 higher CVs were found; especially the FOSAs in air extract pose a problem to many laboratories.

4. Discussion

The interlaboratory assessments coordinated by UNEP in support of the implementation of the Stockholm Convention on POPs have been expanded to include the new POP – PFOS – listed in 2009. Following the recommendation in the guidance document for the GMP, precursor compounds as recommended analytes in air monitoring, have been included as well. Since the analysis of PFASs differs significantly from the analysis of the other more lipophilic chlorinated or brominated POPs, we have included other groups of PFASs besides PFOS into the assessment to allow laboratories to have a broader picture of their performance. In doing so, laboratories and countries are better prepared for the discussion on listing more POPs such as presently discussed for PFOA [15] or PFHxS [16]).

In general it can be concluded after two rounds of interlaboratory assessments that the performance of the PFASs laboratories is similar to that of the dioxin laboratories and the performance is often better than the laboratories analysing for example chlorinated pesticides. In contrast to the dioxin laboratories where 50–60 laboratories participate in the interlaboratory assessments on a regular basis, the number of participating laboratories is still quite low (around 25–30) and the specialization is high. This means that for matrices other than fish or water, only few

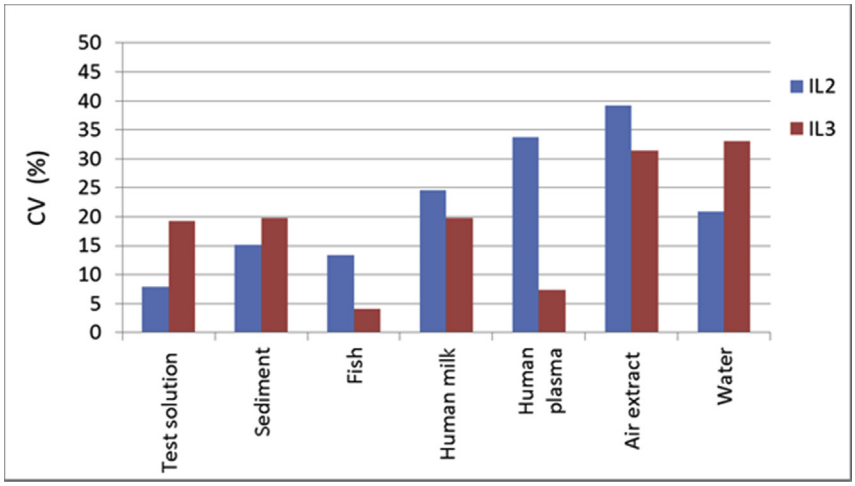

Fig. 1. Comparison between the performance of the analyses of L-PFOS in IL2 and IL3 expressed as coefficients of variation (CV %) *per* type of test sample (as CV).

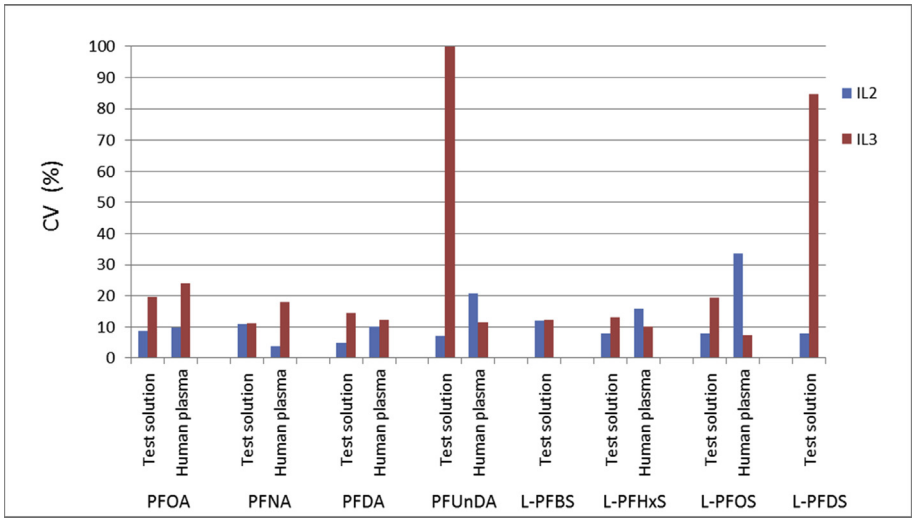

Fig. 2. Comparison between the performance of the analyses of PFASs in test solutions and human plasma in IL2 and IL3 expressed as coefficients of variation (CV %).

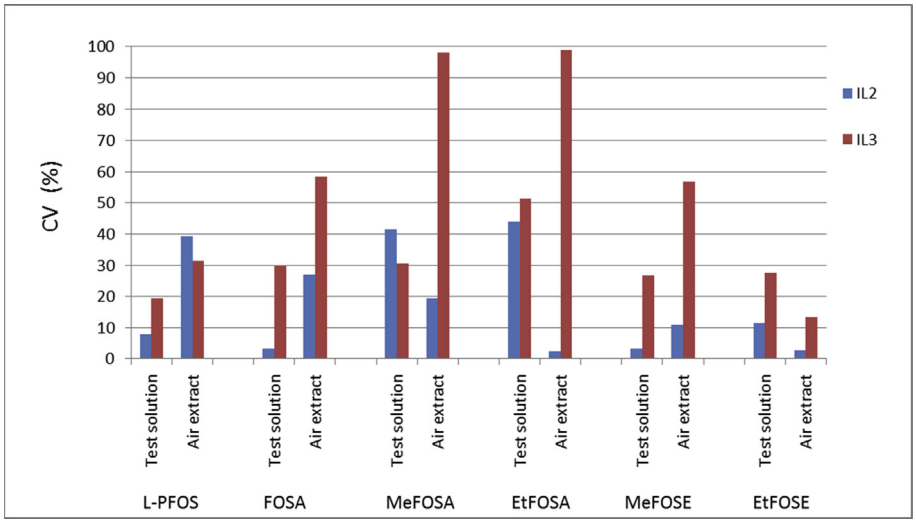

Fig. 3. Comparison between the performance of the analyses of PFOS precursor compounds in test solutions and air extracts in IL2 and IL3 expressed as coefficients of variation (CV %).

laboratories are proficient. Especially the performance for the analysis of L-PFOS is excellent in almost all types of test samples. On the other hand, not all laboratories are used to analyse br-PFOS isomers in general. Therefore, often, no consensus values could be assigned. It has been one of the achievements of these interlaboratory assessments to request the differentiation between L-PFOS and br-PFOS and not only report the total PFOS. All laboratories struggle with the analysis of the precursor compounds – FOSAs and FOSEs [17]. Reported reproducibility coefficients of variation in a range of 7%–31% for surface water and 20%–40% for wastewater for the analysis of perfluoroalkylsubstances (PFASs), including PFOS and PFOA, in water samples by following the protocols of Japanese Industrial Standard (JIS). The authors concluded that the methods tested are robust and reliable and can be used as a standard method for the analysis of target compounds in water samples. We have to emphasize that the present study is hard to compare with the study of Taniyasu et al. [17] because, based on the philosophy that use of various methods reduces systematic errors and makes the dataset stronger, we have left the choice for the method to the participants. In addition, a substantial number of laboratories in the present study originate from developing countries where conditions in laboratories are less appropriate. To improve those is obviously one of our recommendations [18]. Reported CVs for PFOS in human milk of 38%–49% and for PFOA in human milk of 53%–71% (n = 20). They concluded that at that time a clear performance variation was present. While human milk is actually a difficult matrix for PFASs, because these compounds do not bind so much to fat and human milk levels are generally low [19], it is encouraging to see that improvements have been made since 2013, with CV values for PFOS in human milk now being 20%–25%.

Within the Stockholm Convention's GMP on POPs, the regular participation in interlaboratory assessments is encouraged. These proficiency tests have been performed for the fourth time and the last two rounds included the newly listed POPs, i.e. PFASs. Internationally accepted criteria are applied and were further developed to accommodate the requirements under the Convention. One of these criteria is that the UNEP-coordinated exercises that base the z-score on the standard deviation of the dataset with a coefficient

of variation (CV) of ±25% are stricter than most other interlaboratory studies, which often have higher CVs. This means that compared to other studies it is more difficult to obtain satisfactory z-scores in these bi-ennial global interlaboratory assessments. So far, we have defined the z-scores for the test solutions of analytical standards on the same definition (CV = 25%); however, stricter criteria should be applied in the future; i.e. ±10%.

5. Recommendations

For some developing countries it would be recommended to organize a stepwise-designed study with targeted advice on the results. This will however be quite costly, given the large number of laboratories interested. In addition, those countries should then allocate resources to invest in the LC/MS instrumentation needed to perform good quality PFAS analyses and even more into maintenance and acquisition of samples to maintain expertise.

No trends could be observed between methods used in IL2 and IL3. Since detection and identification of more PFASs and even unknown organofluorine components has become more important nowadays, and new PFASs are being found in the environment [20], it would be recommended to include the broader spectrum of at least the fluorinated compounds as was offered here with the test solution of analytical standards and in the human plasma samples also for the other test matrices, i.e. sediment, fish, human milk and air. The low concentrations often found in environmental samples and the larger number of analytes would then need the use of mass spectrometers with higher resolution.

Promising results and some advances in PFASs analysis have been seen with new laboratories participating in the interlaboratory assessment. Further improvements are expected to occur with larger number of samples *per* matrix being analysed so that routines in the laboratories will be set up.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.trac.2019.03.023.

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